

## **DETAILED ACTION**

### ***Application status***

The preliminary amendment to claims, filed on 07/14/2006 is acknowledged, wherein Applicants have added claims 21-39, and canceled claims 1-20.

Claims 21-39 are pending in this application.

### ***Priority***

The instant application is the 371 national stage entry of PCT/FR05/00093, filed on 01/14/2004. The Examiner notes that the requirements of national stage entry of the instant application had been completed (note assigned U.S. filing date) within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to a foreign patent application 0400366 (FRANCE) filed without English translation on 01/15/2004.

### ***Election***

Applicant's election with traverse of Group I, Claims 21-33, and election of species laccase and derivatives thereof, in the response filed on 07/27/09, is acknowledged.

Applicants argue that for filing a patent on an expression system, it is absolutely necessary to have a receiving strain (for the genetic transformation here: the BRFM44

Art Unit: 1656

strain that does not have a laccase activity) and an expression vector that brings an enzymatic production of interest (the proteins of interest). These two elements are linked and are necessary to obtain the recombinant protein of interest. However, these elements are not at all included in the cited prior art, LOMASCOLO et al, 2003 (LOMASCOLO). First, the strain (ss3) used by LOMASCOLO is not genetically modified by the addition of a gene of interest. The ss3 strain already contains a laccase gene that produces the laccase in large quantity, without an inducer. The aim of this study is to point out that the addition, of an inducer (e.g. ethanol) promotes the endogenous laccase gene and increases the enzymatic laccase production to 1 g/L. The work of LOMASCOLO only leads to the obtaining of a native protein. On the contrary, the present invention aims to produce recombinant proteins. Furthermore, the work of LOMASCOLO is based on a set of 1 to 3 endogenous genes of laccase, while the present invention is based on ten or so copies of an exogenous gene of laccase integrated into the genome of the receiving strain. Thus the method of claim 21 clearly indicates that the aim of the present invention is to produce a specific recombinant protein and not a native protein. The two strains are also different because the strain mentioned in LOMASCOLO (ss3) naturally produces a laccase protein, which is not the same as the BRFM44 strain used by the present invention. The BRFM44 strain does not produce naturally laccase, but serves as a receiving host which is transformed to produce recombinant proteins.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. Even if Lomascolo et al. do not teach a genetically

Art Unit: 1656

modified by the addition of a gene of interest, which is not native, Alves et al. (Highly Efficient Production of Laccase-by the Basidiomycete *Pycnoporus cinnabarinus*, APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Nov. 2004, p. 6379-6384, see IDS) specifically teach a method of culturing a genetically modified *P. cinnabarinus* strain which is transformed with an expression vector containing a laccase gene under the control of a promoter (see pages 6379 under "Materials and Methods"), which minimally anticipates claim 21. Therefore, the shared technical feature of the groups is not a "special technical feature", unity of invention between the groups does not exist.

Claims 34-39 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Objections to the Specification***

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in

Art Unit: 1656

compliance, Applicants should identify nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids in the specification by a proper sequence identifier, i.e., "SEQ ID NO:" (see MPEP 2422.01). If these sequences have not been listed in the computer readable form and paper copy of the sequence listing, applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See particularly Figures 4, 5, 7-9 and 12 of the specification containing nucleic acid and amino acid sequences, and therefore, those sequences should be represented by proper sequence identifier numbers in either the Figures themselves or in the Brief Description of the Drawings.

Appropriate correction is required.

### ***Arrangement of the Specification***

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.

Art Unit: 1656

- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
  - (1) Field of the Invention.
  - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

### ***Claim Objections***

Claims 21, 25 and 28-33 are objected to because of the following informalities:

Claims 21, 25 and 28-33 are objected to because recitations of "-" or "\*" can be substantially improved with respect to form. The Examiner suggests replacing the noted symbols with ---(a)..., (b)...,(c)...---, etc or ascending roman numerals.

Appropriate correction is required.

### ***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 (all other claims dependent therefrom) recites the limitation "the gene encoding for this specific protein" in claim 21. There is insufficient antecedent basis for this limitation in the claim. In the interest of advancing prosecution, the noted phrase is interpreted as "a gene encoding for a specific protein".

Claims 21 and 28-33 (all other claims dependent therefrom), the phrase "if appropriate... ", renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). In the interest of advancing prosecution, the noted phrase is not given any patentable weight.

Claims 21, 25 and 33 recite "(also designated as exogenous promoter)", "(halophilic basidiomycete)", "(SEQ ID NO: 18)" and/or "(SEQ ID NO: 17)", which is unclear and indefinite. It is unclear respect to whether or not the recitation inside the parenthesis should be considered as a claim limitation or not. For example, if one interprets "(SEQ ID NO: 18)" as "for example, SEQ ID NO: 18," it renders the claim indefinite because it is unclear whether the limitation inside the parenthesis is part of the claimed invention. See MPEP § 2173.05(d). In the interest of advancing prosecution, the noted phrase is not given any patentable weight.

Claims 24, 25 and 28 recite the phrase, "such as ...", which is unclear and indefinite. It is unclear respect to whether the limitation(s) following the phrase are part

Art Unit: 1656

of the claimed invention. See MPEP § 2173.05(d). In the interest of advancing prosecution, the noted phrase is not given any patentable weight.

Claim 32 recites the phrase "the nucleotide sequence delimited by the nucleotides situated at positions 128 and 190 of SEQ ID NO: 1 encoding for the peptide signal of *Pycnoporus cinnabarinus* delimited by the first 21 amino acids of SEQ ID NO: 2", which is unclear and indefinite. It is unclear as to what this phrase means. In the interest of advancing prosecution, the noted phrase is not given any patentable weight.

### ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 21-31 are rejected under 35 U.S.C. § 102(a) as being anticipated by Alves et al. (Highly efficient production of laccase by the Basidiomycete *Pycnoporus cinnabarinus*, Applied and Environmental Microbiology, Vol. 70, No. 11, Nov. 2004, pp: 6379-6384, see IDS) as evidenced by Herpoel et al. (Selection of *Pycnoporus cinnabarinus* strains for laccase production, FEMS Microbiology Letters, 183, (2000), pp: 301-306, see IDS).

The instant claims are drawn to a method for preparing a specific recombinant protein, said method being carried out by overexpression of the gene encoding for this specific protein in a monokaryotic strain of filamentous fungi of the species *Pycnoporus*

Art Unit: 1656

of the basidiomycete group, and comprises: (a) a stage of culturing the abovementioned monokaryotic strain of *Pycnoporus*, said strain being transformed using an expression vector containing the gene encoding for the specific recombinant protein, the expression of which is placed under the control of a promoter corresponding to an endogenous promoter of the abovementioned fungi, or of a different promoter, said promoter being constitutive or inducible, and (b) the recovery. See above rejections under 112 2<sup>nd</sup> paragraph, and claims objections for the claim interpretation.

Alves et al. teach a method of over-expressing laccase, specifically lac1 from *Pycnoporus cinnabarinus*, which is identical to Applicants' SEQ ID NO: 2 (see below sequence alignment, Qy = Applicants' SEQ ID NO: 2 and Db = the amino acid sequence corresponding to GenBank accession number AF170093 of Alves et al. as disclosed on page 6380, left column under "Construction of laccase expression vectors"), in the monokaryotic laccase-deficient *Pycnoporus cinnabarinus* strain BRFM44, said method comprising culturing said strain transformed with an expression vector, wherein the expression is placed under the control of the endogenous promoter of the said laccase (also known as *pLac* promoter), *sc3* promoter of *Schizophyllum commune*, or *gdp* promoter of *Schizophyllum commune*, wherein said laccase is labeled with histidine tag (see under "MATERIALS AND METHODS" ON PAGES 6379-6380). It is noted by the Examiner that claim 22 only describes characteristics of how the monokaryotic *Pycnoporus cinnabarinus* was obtained, which is inherent characteristics of the monokaryotic laccase-deficient *Pycnoporus cinnabarinus* strain BRFM44. In support of this notion, it is noted by the Examiner that the method of obtaining



Art Unit: 1656

monokaryotic strains of *Pycnoporus cinnabarinus* as recited in claim 22 was routine in the prior art as evidenced by Herpoel et al. (Selection of *Pycnoporus cinnabarinus* strains for laccase production, FEMS Microbiology Letters, 183, (2000), pp: 301-306, see IDS). Therefore, teachings of Alves et al. anticipate claims 21-31.

```

RESULT 1
Q9UVQ2_PYCCI
ID   Q9UVQ2_PYCCI                Unreviewed;          518 AA.
AC   Q9UVQ2;
DT   01-MAY-2000, integrated into UniProtKB/TrEMBL.
DT   01-MAY-2000, sequence version 1.
DT   14-OCT-2008, entry version 38.
DE   SubName: Full=Laccase;
DE   EC=1.10.3.2;
GN   Name=Lac1; Synonyms=lac1;
OS   Pycnoporus cinnabarinus (Cinnabar-red polypore).
OC   Eukaryota; Fungi; Dikarya; Basidiomycota; Agaricomycotina;
OC   Agaricomycetes; Polyporales; Polyporaceae; Pycnoporus.
OX   NCBI_TaxID=5643;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RC   STRAIN=I-937;
RX   MEDLINE=20177685; PubMed=10712591;
RX   DOI=10.1046/j.1432-1327.2000.01166.x;
RA   Otterbein L., Record E., Longhi S., Asther M., Moukha S.;
RT   "Molecular cloning of the cDNA encoding laccase from Pycnoporus
RT   cinnabarinus I-937 and expression in Pichia pastoris.";
RL   Eur. J. Biochem. 267:1619-1625(2000).
RN   [2]
RP   NUCLEOTIDE SEQUENCE.
RC   STRAIN=I-937;
RA   Otterbein L., Record E., Moukha S.;
RT   "Cloning of a cDNA encoding laccase protein from Pycnoporus
RT   cinnabarinus I-937.";
RL   Submitted (MAY-1999) to the EMBL/GenBank/DDBJ databases.
CC   -----
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   -----
DR   EMBL; AF170093; AAF13052.1; -; Genomic_DNA.
DR   EMBL; AF152170; AAG13724.1; -; mRNA.
DR   HSSP; Q96UT7; 1KYA.
DR   SMR; Q9UVQ2; 22-517.
DR   GO; GO:0005507; F:copper ion binding; IEA:InterPro.
DR   GO; GO:0008471; F:laccase activity; IEA:EC.
DR   GO; GO:0055114; P:oxidation reduction; IEA:UniProtKB-KW.
DR   InterPro; IPR001117; Cu-oxidase.
DR   InterPro; IPR011706; Cu-oxidase_2.
DR   InterPro; IPR011707; Cu-oxidase_3.
DR   InterPro; IPR002355; Cu_oxidase_Cu_BS.
DR   InterPro; IPR008972; Cupredoxin.
DR   Gene3D; G3DSA:2.60.40.420; Cupredoxin; 3.
DR   Pfam; PF00394; Cu-oxidase; 1.
DR   Pfam; PF07731; Cu-oxidase_2; 1.
DR   Pfam; PF07732; Cu-oxidase_3; 1.
DR   PROSITE; PS00079; MULTICOPPER_OXIDASE1; 1.
PE   2: Evidence at transcript level;

```

Art Unit: 1656

KW Copper; Metal-binding; Oxidoreductase.

SQ SEQUENCE 518 AA; 56292 MW; 329714CF463ED081 CRC64;

Query Match 100.0%; Score 2779; DB 2; Length 518;

Best Local Similarity 100.0%;

Matches 518; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

Qy      1 MSRFQSLFFVVLVSLTAVANAAIGPVADLTLTNAQVSPDGFAREAVVVGITPAPLITGN 60
        |||
Db      1 MSRFQSLFFVVLVSLTAVANAAIGPVADLTLTNAQVSPDGFAREAVVVGITPAPLITGN 60

Qy     61 KGDRFQLNVIDQLTNHTMLKTSSIHWHGFFQQGTNWADGPAFVNQCPIASGHSFLYDFQV 120
        |||
Db     61 KGDRFQLNVIDQLTNHTMLKTSSIHWHGFFQQGTNWADGPAFVNQCPIASGHSFLYDFQV 120

Qy    121 PDQAGTFWYHSHLSTQYCDGLRGPVVYDPNDPHASLYDIDNDDTVITLADWYHVAAKLG 180
        |||
Db    121 PDQAGTFWYHSHLSTQYCDGLRGPVVYDPNDPHASLYDIDNDDTVITLADWYHVAAKLG 180

Qy    181 PRFFPGSDSTLINGLGRITGIAPSDLAVIKVTQKRYRFRVLVSLSCDPNHTFSIDNHTMT 240
        |||
Db    181 PRFFPGSDSTLINGLGRITGIAPSDLAVIKVTQKRYRFRVLVSLSCDPNHTFSIDNHTMT 240

Qy    241 IIEADSINTQPLEVDSIQIFAAQRYSFVLDA SQPVDNYWIRANPAFGNTGFAGGINSAIL 300
        |||
Db    241 IIEADSINTQPLEVDSIQIFAAQRYSFVLDA SQPVDNYWIRANPAFGNTGFAGGINSAIL 300

Qy    301 RYDGAPEIEPTSVQTTPTKPLNEVDLHPLSPMPVPGSPEPGGVDKPLNLVFNFGTNTFFI 360
        |||
Db    301 RYDGAPEIEPTSVQTTPTKPLNEVDLHPLSPMPVPGSPEPGGVDKPLNLVFNFGTNTFFI 360

Qy    361 NDHTFVPPSVPVLLQILSGAQAAQDLVPEGSVFVLPSNSSIEISFPATANAPGFPHPFHL 420
        |||
Db    361 NDHTFVPPSVPVLLQILSGAQAAQDLVPEGSVFVLPSNSSIEISFPATANAPGFPHPFHL 420

Qy    421 HGHAFAVVRSAAGSSVYNDNPIFRDVVSTGQPGDNVTIRFETNPNPGPWFLHCHIDFHLDA 480
        |||
Db    421 HGHAFAVVRSAAGSSVYNDNPIFRDVVSTGQPGDNVTIRFETNPNPGPWFLHCHIDFHLDA 480

Qy    481 GFAVMAEDTPDTKAANPVPQAWSDLCPDYDALDPSDL 518
        |||
Db    481 GFAVMAEDTPDTKAANPVPQAWSDLCPDYDALDPSDL 518

```

### ***Claim Rejections - 35 U.S.C. § 103***

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 21-32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lomascolo et al. (Overproduction of laccase by a monokaryotic strain of *Pycnoporus*

Art Unit: 1656

*cinnabarinus*, Journal of Applied Microbiology, 94, pp: 618-624, see IDS) in view of Halaouli et al. (Characterization of a new tyrosinase from *Pycnoporus* species with high potential for food technological applications, Journal of Applied Microbiology, published online in Nov. 2004, 98, pp: 332-343), KSR International Co. v. Teleflex Inc., 550 U.S.--, 82 USPQ2d 1385 (2007), and the evidentiary references of Herpoel et al. (Selection of *Pycnoporus cinnabarinus* strains for laccase production, FEMS Microbiology Letters, 183, (2000), pp: 301-306, see IDS) and Alves et al. (Highly efficient production of laccase by the Basidiomycete *Pycnoporus cinnabarinus*, Applied and Environmental Microbiology, Vol. 70, No. 11, Nov. 2004, pp: 6379-6384, see IDS).

The instant claims are drawn to a method for preparing a specific recombinant protein, said method being carried out by overexpression of the gene encoding for this specific protein in a monokaryotic strain of filamentous fungi of the species *Pycnoporus* of the basidiomycete group, and comprises: (a) a stage of culturing the abovementioned monokaryotic strain of *Pycnoporus*, said strain being transformed using an expression vector containing the gene encoding for the specific recombinant protein, the expression of which is placed under the control of a promoter corresponding to an endogenous promoter of the abovementioned fungi, or of a different promoter, said promoter being constitutive or inducible, and (b) the recovery. See above rejections under 112 2<sup>nd</sup> paragraph, and claims objections for the claim interpretation.

Lomascolo et al. teach a method comprising (I) culturing *Pycnoporus cinnabarinus* to over-express laccase by the use of monokaryotic strain, *Pycnoporus cinnabarinus* ss3 (see page 619, left column under "Fungal strains"), and (II) purification

Art Unit: 1656

of said laccase (see page 619-620, right column under “Laccase purification and N-terminal amino acid sequence determination). Furthermore, Lomascolo et al. identified the monokaryotic strain, “*P. cinnabarinus* ss3 as an outstanding producer of laccase” (see page 618 under “Abstract”). Lomascolo et al. do not teach the use of expression vector containing promoter and histidine tag to over-express said laccase. Lomascolo et al. do not teach the tyrosinase of *Pycnoporus sanguineus* as recited in claim 32.

Halaouli et al. teach characterization of a new tyrosinase from *Pycnoporus sanguineus* with high potential for food technological applications. Halaouli et al. further teach that “among the genus *Pycnoporus*, known for the production of laccase, the strain *P. sanguineus* CBS 614.73 was shown to produce one other phenoloxidase, a new monomeric tyrosinase with a specific activity of 30 and 84 U mg<sup>-1</sup> protein for monophenolase and diphenolase respectively” (see page 332 under “Abstract”). Halaouli et al. identified *P. sanguineus* CBS 614.73 as a potential producer of a tyrosinase which demonstrated effectiveness in the synthesis of antioxidant molecules and in protein cross-linking. It is noted by the Examiner that said tyrosinase isolated from *P. sanguineus* CBS 614.73 must be identical to Applicants' SEQ ID NO: 16 based on the fact that the amino acid sequence of said tyrosinase determined by Halaouli et al., “IVTGPVGGQTEGAPAPNR” is identical to residue 4-22 of SEQ ID NO: 16. Halaouli et al. further teach that some of *Pycnoporus cinnabarinus* strains MUCL 29375, MUCL38480, I-937 and ss3 as recited in Table 1 are outstanding producers of tyrosinases (see page 334).

Art Unit: 1656

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to practice the method of culturing monokaryotic strain of *Pycnoporus cinnabarinus*, i.e., ss3, as taught by Lomascolo et al. and insert the laccase gene or the tyrosinase gene as taught by Halaouli et al. in an expression vector comprising a promoter and an affinity tag to over-express said gene because such *Pycnoporus cinnabarinus* strain has been identified by Lomascolo et al. and Halaouli et al. as an outstanding producer of said enzymes. One of ordinary skill in the art would have motivated to practice such methods because [i] placing said gene under the control of a promoter, and deleting the corresponding endogenous gene would make optimization and control of the over-expression of said genes easier, and [ii] tagging the encoded proteins with an affinity tag, i.e., histidine tag, would make the subsequent purification of the encoded proteins easier. Furthermore, there is a high expectation of success for practicing such methods because [a] methods for obtaining monokaryotic strain of *Pycnoporus cinnabarinus* as recited in claim 22 was routine in the prior art as evidenced by Herpoel et al. (Selection of *Pycnoporus cinnabarinus* strains for laccase production, FEMS Microbiology Letters, 183, (2000), pp: 301-306, see IDS), and [b] methods for over-expressing laccases via use of expression vectors comprising a promoter and an affinity tag was routine in the prior art as evidenced by Alves et al. (Highly efficient production of laccase by the Basidiomycete *Pycnoporus cinnabarinus*, Applied and Environmental Microbiology, Vol. 70, No. 11, Nov. 2004, pp: 6379-6384, see IDS and above rejection under 35 USC 102). While a single reference might not teach a specific embodiment of the claimed methods, the combination of references as

Art Unit: 1656

noted above does disclose that the use of an expression vector comprising a promoter and an affinity tag for the expression of laccases and tyrosinases in a monokaryotic strain of *Pycnoporus cinnabarinus* as being appropriate. As discussed in KSR International Co. v. Teleflex Inc., 550 U.S.--, 82 USPQ2d 1385 (2007), it is considered obvious to combine prior art elements known to be used in equivalent fields of endeavor together into a single combination. The references clearly show that the claimed methods were known to be used in equivalent fields of endeavor; thus, it is considered obvious to combine them together. For the reasons described above, the claimed methods are *prima facie* obvious over the combined teachings of the prior art.

### **Conclusion**

Claims 21-33 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in this Office action to be fully responsive in prosecution.

The instant Office action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on M-F between 9:00-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1656

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JAE W LEE/  
Examiner, Art Unit 1656

/SUZANNE M. NOAKES/  
Primary Examiner, Art Unit 1656